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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Reiner Grabowski

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04/06/2006

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EXAMINER

CALAMITA, HEATHER

ART UNIT

PAPER NUMBER

1637

DATE MAILED: 04/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/088,966	Applicant(s) GRABOWSKI ET AL.	
	Examiner Heather G. Calamita, Ph.D.	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 86,88,89,92-94,96,97,100,102,105 and 107 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 86,88,89,92-94,96,97,100,102,105 and 107 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 13, 2006, has been entered.

Status of Application, Amendments, and/or Claims

2. Claims 86, 88, 89, 92, 93, 94, 96, 97, 100, 102, 105 and 107 are currently pending and under examination. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 86, 88, 89, 92, 93, 94, 96, 97, 100, 102, 105 and 107 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common

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attributes or features of the elements possessed by the members of the genus in view of the species disclosed.” (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

The current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. Applicant has express description for SEQ ID NOs: 2 and 78 not the hundreds of nucleic acid sequences that are complements of or have 70% or 90% identity to SEQ ID NOs: 2 and 78. Thus, applicant has express possession of only 2 specific nucleic acids, namely SEQ ID NOs: 2 and 78, in a genus which comprises hundreds of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains.

No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

“A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. “

In the current situation, complements of or 70% or 90% identity to SEQ ID NOs: 2 and 78 is precisely the situation of naming a type of material which is generally known to likely exist, is in the absence of knowledge of the material composition and fails to provide descriptive support for

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the generic claim.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely by its functional utility, as a nucleotide sequence, without any definition of the particular changes due to selectively hybridizing language claimed.

In the instant application, certain specific nucleotide sequences are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids with a particular sequence. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 86, 88, 89, 92-94, 96-98, 102, 105 and 107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al. (USPN 5,654,141, 08/05/1997) in view of Yamamoto et al. (Genebank Accession number AB001341, submitted January 25, 1997).

With regard to claim 86, Mariani et al. teach a method for detecting an enterobacteria in an analytical sample, comprising

the step of bringing the analytical sample into contact with an added nucleic acid or a combination of added nucleic acids, and detecting suitable hybrid nucleic acids comprising at least one of the added nucleic acids and bacterial nucleic acids wherein the one or more added nucleic acid is SEQ ID NO:2 (see col. 2 lines 10-16, and see col. 2 lines 52 and 54 and example 1, where *E. coli* are enterobacteria).

With regard to claims 88 and 93, Mariani et al. teach the process involves a PCR amplification of the nucleic acid to be detected (see col. 5 lines 40-44).

With regard to claims 89 and 94, Mariani et al. teach in that the process involves a Southern Blot hybridization (see col. 8 lines 8-9).

With regard to claims 92 and 105, Mariani et al. teach a method for amplifying bacterial DNA of a multiplicity of different taxonomic units, especially genera and species, using primers in which in a first amplification step the DNA for high taxonomic units such as classes, phyla or families is amplified with conserved primers (see col. 4 lines 21-29, and 38-43, where the 16S rRNA gene is conserved, and the target nucleic acids are from the classes of *Escherichia*, *Streptococcus*, *Staphylococcus* and *Bacteroides*). And, optionally, in a further step, the DNA fragments obtained by amplification which are specific for genera or species are detected by means of probes, wherein the primers used comprise SEQ ID NO: 2 (see col. 8 lines 39-56).

With regard to claim 97, Mariani et al. teach the one or more added nucleic acid molecule or molecules is modified or labeled so that it can generate a signal in analytical detection procedures, with the modification being fluorescent (see col. 8 lines 1-20).

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With regard to claim 107, Mariani et al. teach the modified or labeled groups are substances with affinity to enzymes or enzyme complexes (see col. 6 lines 53-54, where biotin is a substance with affinity to enzymes or enzyme complexes).

With regard to claims 86, 88, 89, 92-94, 96-98, 102 and 105, Mariani et al. do not teach SEQ ID NO 2.

Yamamoto et al. teach SEQ ID NO 2 and sequences with 90% identity to SEQ ID NO:2 (see alignment below).

Claimed SEQ ID NO: 2 1 ttcgggtgtcatgccaatg 20

Yamamoto et al. 11799 ttcgggtgtcatgccaatg 11780

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Mariani with the use of functionally equivalent nucleic acid selected from the sequence of Yamamoto since Mariani expressly teaches primer selection using primers which amplify specific sequences in *E. coli* in order to detect the presence of the bacteria in patient samples.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers for the detection of *E. coli* and concerning which a microbiologist of ordinary skill would attempt to obtain alternate compounds

with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Response to Arguments

5. Applicant's arguments filed February 13, 2006, have been fully considered but they are not persuasive.

With respect to the Mariani reference, Applicants argue that Mariani do not teach a method of detecting a taxonomic unit of enterobacteria as recited in the preamble of the method claims. This is not persuasive because Mariani teach the method steps of the claims and the preamble simply recites the intended use of the method. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a

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structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). See MPEP 2111.02 for discussion on the determination of weight given to the preamble.

Applicants argue the 103 (a) rejection of the claims is improper because the rationale amounts to an invitation to experiment or an obvious to try situation and possibly involves hindsight reasoning. This is not persuasive because Buck shows every 18 mer primer selected over 300 base pairs was successful. This leads to the expectation of success for amplification or extensions. In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers for the detection of *E. coli* and concerning which a microbiologist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations and the 103 (a) rejections are proper and therefore maintained.

Allowable Subject Matter

6. The following is a statement of reasons for the indication of allowable subject matter:

SEQ ID NO: 78 is free of the prior art.

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Summary

7. No claims were allowable.

Correspondence

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

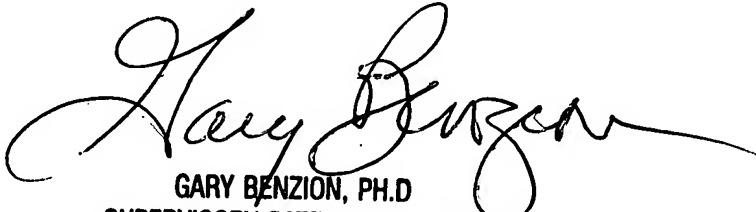
Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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